REMARKS

A check for the fees for an extension of time for an additional three months extension of time accompanies this response. Any fees that may be due in connection with filing this paper or with this application during its entire pendency may be charged to Deposit Account No. 06-1050. If a Petition for extension of time is required, this paper is to be considered such Petition, and any fee charged to Deposit Account No. 06-1050.

Claims 1, 3-32, 34-47, 59, 61-64 and 144-147 are pending in this application. Claims 1, 3-25, 27-32, 35-47 and 144-146 are allowable. Claim 26 and 34 are amended herein for clarity as suggested by the Examiner. Claim 59 is amended to depend from allowable claim 1, thereby obviating any rejection thereof. It respectfully is submitted that the amendments herein should place the application into condition for allowance.

Applicant also is submitting a Supplemental Information Disclosure Statement filed under separate cover on the same day as the instant amendment and response.

Applicant, however, maintains that, as discussed previously, the Examiner has failed to provide any documentation to support the concept that serum-free medium is a delivery agent and/or that it increases permeability of cells. Serum free medium is employed to suspend cells and to maintain their viability; there is no evidence of record that serum free medium enhances contact of a nucleic acid with a cell or increases permeability of cell. As discussed in the previous responses, serum free medium is employed with a delivery agent, such as LIPOFECTAMINE, and is not, by itself, something that delivers a nucleic acid molecule into a cell. The instructions for use of LIPOFECTAMINE and for TRANSFECTAM specifically require suspension of cells in serum free medium; there is no evidence of record that one of ordinary skill in the art would consider serum free medium to be a delivery agent by itself. The application describes the use of two delivery agents, and exemplifies using LIPOFECTAMINE as **one of the agents**. Using LIPOFECTAMINE in accord with the manufacturer's instructions **does not constitute** use of two reagents.

Again, the Examiner is reminded MPEP 2144.03 states:

> The Examiner may take official notice of facts outside of the record which are capable of instant and unquestionable demonstration as being "well- known" in the art. In re Ahlert, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970). . . ..

The statement by the Examiner that the serum free medium in which the cells are suspended increases permeability is not capable of instant and unquestionable demonstration. MPEP 2144.03 continues:

> If justified, the examiner should not be obliged to spend time to produce documentary proof. If the knowledge is of such notorious character that official notice can be taken, it is sufficient so to state. In re Malcolm, 129 F.2d 529, 54 USPQ 235 (CCPA 1942). If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position.

In this instance, there is no evidence serum-free medium is used to increase permeability of cells nor evidence that such knowledge is notorious. As discussed previously, serum-free medium or other medium is employed because the instructions for use of cationic lipid delivery agents requires suspension of the cells. Furthermore, cells must be suspended in a medium suitable for maintaining viability. Serum-free medium is employed to maintain viability; it is not a delivery agent.

The Examiner has never addressed these failures to provide evidence and documentation. On appeal to the Board, the Board would deem it to be an error to base a rejection on unsupported supposition that goes against the art of record. Hence, Applicant maintains that the Examiner's interpretation of delivery agent as including the medium in which a cell is suspended, merely because it includes some components in common with delivery agents, is untenable and unsupported. Merely because serum free medium includes some components that are, when applied in high concentrations, delivery agents, does not make serum free medium a delivery agent within the scope of any definition of a delivery agent. Serum free medium is not and would not be recognized by any one of ordinary skill in the art to constitute a delivery agent; the Examiner has provided no evidence that serum free medium delivers nucleic acid molecules into cells. As discussed in the previous response and below, suspension in serum free medium is part of the manufacturer's protocol for applying a commercial delivery agent. Addition of serum free medium is part of the protocol for adding a cationic amine to cells. It serves as the medium in which cells are suspended for addition of the cationic amine; there is nothing to indicate that the medium serves as a delivery agent; it is not a separate delivery. As interpreted by the Examiner, the claims, as previously pending, read on addition of a single delivery agent. The specification and claims render it clear that two reagents are required.

Notwithstanding this, this **issue is not relevant** to the presently rejected claims, claims 59 and dependents, which recite the use of a composition containing DOPE and DOSPA (LIPOFECTAMINE). As amended, claim 59 and dependents recite all elements of allowable claim 1.

THE REJECTION OF CLAIMS

Claims 59, 61-64 and 147 are rejected under 35 U.S.C. §103(a) as being upatentable over Hadlaczky *et al.* (U.S. Patent No. 6,025,155), which teaches lipid-mediated transfection, in view of Marschall *et al.* as evidenced by LIPOFECTAMINE Reagent or TRANSFECTAM Reagent because Hadlaczky *et al.*, describes introduction of artificial chromosomes, including ACES, into cells using lipid mediated transfer; and Marschall *et al.* teaches use of the commercially available cationic amines, LIPOFECTAMINE and TRANSFECTAM for introduction of YACS into cells. The Examiner concludes that it would have been obvious to have used LIPOFECTAMINE or TRANSFECTAM for lipid-mediated transfection of large nucleic acid molecules, such as ACES into cells. This rejection is respectfully traversed.

It is respectfully submitted that amendment of claim 59 to depend from allowable claim 1 renders this ground for rejection moot.

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In view of the above amendments and remarks, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,

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